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Rejection Pursuant to 35 U.S.C. 102(e):

The Examiner rejected claims 4 through 8 and 10 through 17 under 35 U.S.C. 102(e) as being anticipated by the compound of structure II of Tao et al. U.S. Patent No. 5,780,653.

To overcome this rejection, Applicants file herewith the attached copy of the Order and Memorandum Opinion dated October 31, 2001, by U.S. District Court Judge Roger Vinson of the Northern District of Florida, Tallahassee Division. This Opinion followed a nine-day trial before the Court and sets forth extensive findings of fact and conclusions of law.

In particular, the Opinion explains the history through 1994 whereby Applicants synthesized taxoltere PNIP and taxoltere metro. (*See* the Opinion *generally* at pages 2-8) Through their biological testing which culminated in an October 27, 1994, memorandum providing the test results, Applicants proved the ability of taxoltere PNIP and taxoltere metro to kill cancer cells. (*See* the Opinion at page 8)

Applicants believe the Opinion is sufficient proof for them to get behind Tao, et al. Since the Opinion is on appeal and even though Applicants believe a reversal of the fact findings cited above is remote, they are currently preparing a Section 131 affidavit and proofs to independently swear behind Tao, et al. They will submit this declaration shortly.

Since each of claims 4 through 8 and 10 through 17 reads on taxoltere PNIP and/or taxoltere metro, and since the primary use for the biological testing of such compounds as found in the Opinion is to identify compounds which kill cancer cells in humans, the Opinion proves that Applicants conceived and reduced to practice each of claims 4 through 8 and 10 through 17 no later than October 27, 1994 – well before the filing date of the Tao patent, June 7, 1995. As such, the rejection of claims 4 through 8

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and 10 through 17 under 35 U.S.C. 102(e) has been overcome and should be withdrawn.

As for claim 9, nothing in Tao et al. discloses or teaches the metal complex required by claim 9. As such, regardless of dates of invention, claim 9 is patentable over Tao, et al. and should be allowed at this time.

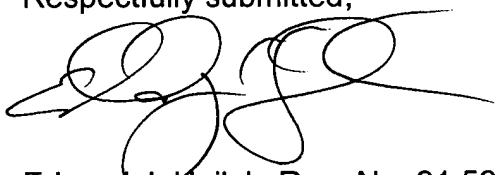
In view of the foregoing, favorable reconsideration is respectfully requested. If the Examiner wishes to discuss any aspect of this application, he is invited to telephone the undersigned attorney for discussion.

A check in the amount of $400.00 for a two month extension of time is enclosed.

CONCLUSION

Favorable consideration and allowance of all pending claims is requested. The Commissioner is hereby authorized to charge any deficiency or overpayment of the required fee to Deposit Account No. 19-1345.

Respectfully submitted,



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DGL/EJH/vlm
*Attachments

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IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF FLORIDA
TALLAHASSEE DIVISION

THE BOARD OF EDUCATION, a corporate body of the State of Florida, for and on behalf of the Board of Trustees of Florida State University; MDS RESEARCH FOUNDATION, INC., a non-profit Florida foundation; and TAXOLOG, INC. a Delaware corporation,

Plaintiffs,

v. Case No. 4:99cv131/RV

AMERICAN BIOSCIENCE, INC., a California corporation formerly known as VIVORX PHARMACEUTICALS, INC., and CHUNLIN TAO, an individual,

Defendants.

_____/

ORDER AND MEMORANDUM OPINION

In this action, the plaintiffs Board of Education (on behalf of the Board of Trustees of Florida State University); MDS Research Foundation, Inc.; and Taxolog, Inc. seek a declaration correcting the named inventors on U.S. Patent No. 5,780,653 ("'653 patent"). They also seek a declaratory judgment that this patent is

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unenforceable because it was obtained by inequitable conduct.[1] The patent at issue claims three chemical Taxol-related compounds with both cytotoxic and radiosensitizing properties that can be used to combat certain types of cancer cells.

This case was tried before the Court, without a jury, in a nine-day trial. After considering the pleadings, the parties' stipulations, all the evidence in the record, and the arguments of counsel at trial, I conclude that the plaintiffs have proved by clear and convincing evidence that the '653 patent names the incorrect inventors and that the patent was obtained by inequitable conduct. As is required by Rule 52, Federal Rules of Civil Procedure, I make the following findings of fact and conclusions of law.

I. FINDINGS OF FACT

Approximately thirty years ago it was discovered that a naturally-occurring compound, identified as "taxol," isolated from the bark of the pacific yew tree, demonstrated an ability to shrink certain types of cancer tumors. However, the extraction of natural taxol from the bark of the yew tree was extremely expensive and provided only a small yield of the compound. Moreover, the process required removal of the yew tree's bark, which killed the tree. By the late 1980s, when it was confirmed that taxol could serve as a potent anti-cancer drug, it was recognized that supplying the medical need would be difficult because the supply of yew bark was quite limited and it required a large quantity of bark to produce only a few grams of taxol. Additionally, an intensive environmental campaign was underway to protect the yew trees from being harvested for the production of taxol. Due to these economic,

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[1]This action originally consisted of seven counts against defendants American Bioscience, Inc. ("ABI") and Chunlin Tao. Count III was dismissed (doc. 155) and summary judgement was entered in favor of the defendants as to Counts I, II, IV, V, and VI of the claims asserted by MDS Research Foundation, Inc. ("MDS") and Taxolog, Inc. (doc. 265). Finally, pursuant to Rule 68 of the Federal Rules of Civil Procedure, the defendants' offer of judgment was accepted by FSU and judgment entered as to Counts I, II, IV, V, and VI of the claims asserted by the Board of Education, for and on behalf of the Board of Trustees of Florida State University (doc. 396). Thus, only Count VII remained for trial, and only the claims of Count VII are addressed in this order.

environmental, and natural factors, worldwide interest existed in both the scientific and medical-pharmaceutical communities to develop a synthetic taxol. Groups of scientists in the United States and elsewhere mobilized to attempt to achieve the total synthesis of the complex taxol molecule. One of these teams was led by Dr. Robert Holton at Florida State University ("FSU") in Tallahassee, Florida.

From the mid-1980s through the early 1990s, Dr. Robert Holton worked with other scientists, first at Virginia Polytechnic University ("Virginia Tech") and subsequently at FSU, to develop a process for creating synthetic taxol in the laboratory. To assist in his research, FSU had authorized Dr. Holton to hire post-doctoral research assistants to conduct research and be a part of his team of scientists. Initially, Dr. Holton's team efforts were focused on synthesis of the complex taxol rings. Eventually, Dr. Holton's team of 15-20 scientists began to focus on the total synthesis of taxol by attaching the side-chain at the C-13 position of the ring structure. (See diagram of Taxol molecule, Attachment A) Their efforts were successful, and they won the worldwide race to produce taxol in the laboratory. On December 9, 1993, Dr. Holton and his team at FSU celebrated their achievement of being the first to accomplish the total synthesis of taxol. Through FSU, they obtained a patent and licensed the product to Bristol Myers Squibb Pharmaceuticals, Inc. ("BMS"). In 1994, BMS announced that it was manufacturing and marketing the synthetic taxol created at FSU,[2] in lieu of natural taxol.

Once the tremendous potential of this compound was realized, Dr. Holton directed his team's efforts into developing more effective variations of taxol, known as taxol analogs or taxanes, that were believed to have even more effective cancer-fighting properties. Even while they were working on the total taxol synthesis, Dr. Holton and his team at FSU had been pursuing the development of taxol analogs ("the

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[2]FSU had entered into a licensing agreement with BMS, and the synthetic taxol marketed by BMS has produced well over $150 million in royalties for FSU between 1995 and 2000.

analog program"), which ran parallel to and overlapped with the total synthesis project. After his 1993 success in the total taxol synthesis, Dr. Holton's team concentrated on research involving the various taxol analogs. This case concerns the true inventorship of a patent for taxol analogs obtained by one of Dr. Holton's former research assistants, Dr. Chunlin Tao.

On July 17, 1992, Dr. Holton had hired Dr. Chunlin Tao, a Chinese national, as a post-doctoral research assistant in his laboratory.[3] Pursuant to his employment with FSU, Dr. Tao signed an intellectual property agreement in which he agreed, inter alia, to retain as confidential all proprietary information learned at FSU and to not disclose any confidential information or trade secrets to any third party.[4] While employed by FSU, Dr. Tao worked on both the total taxol synthesis project and on the taxol analogs project. Dr. Tao worked in Dr. Holton's laboratory at FSU from July 1992 to November 1994, at which time he left to begin working for VivoRx, Inc. in California.[5]

Generally, Dr. Holton and his research assistants at FSU met in daily, or at least weekly, group sessions to discuss the difficulties encountered and the successes achieved by the other members of Dr. Holton's team. These meetings were free flowing conversations in which all the members participated and collaborated. The

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[3]Chunlin Tao had received his undergraduate training in chemistry in China, as well as a masters degree in organic chemistry. He then came to the United States and earned his Ph.D. at Marquette University in Milwaukee, Wisconsin. He left Marquette to join Dr. Holton's team at FSU as a post-doctoral student. Before arriving at FSU, Dr. Tao had no background in cancer research, taxol, taxanes, radiation biology, or radiosensitizers.

[4]According to Dr. Tao, he signed this intellectual property agreement at the same time that he signed numerous other forms, such as health insurance forms and forms required for employment at FSU. Dr. Tao testified that he did not realize what he was signing and did not read this agreement. Consequently, he felt that he was free to use the knowledge and training gained during his time at FSU at his new job in California.

[5]VivoRx, Inc. was a parent company to VivoRx Pharmaceuticals, Inc. (American Bioscience Inc.'s predecessor), but Dr. Tao performed duties for both companies.

research done by any member of the team was required to be made available for any other member to see and use. All of Dr. Holton's research assistants were directed to leave their lab books out on their desks for other team members to review their present or past lab work. Dr. Holton would identify the analogs or compounds that he wanted his research assistants to attempt to synthesize, and because of the collaborative environment of the laboratory, each team member knew what research the others were conducting. Thus, as a member of FSU's research team, Dr. Tao had open access to the discoveries, research, and knowledge of all the other team members.

In 1992, Dr. Hossain Nadizadeh, while also employed as a post-doctoral research member of Dr. Holton's team at FSU, synthesized a taxane having a paranitrophenyl ring at the 3' position of the side-chain and a t-butoxy-carbonyl at the N position of the side-chain. This ultimate taxane was known as FSU's "PNIP." To achieve the attachment of the PNIP side chain at the C-13 position at the desired yield of the final product, Dr. Nadizadeh had to develop and employ a new alternative attachment method.

The process of attaching the side-chain of a taxol analog requires the creation of a "beta lactam." A beta lactam is a particularized methodology for protecting some parts of the molecule while getting a desired attachment at a particular location. Beta lactams are not commercially available and must be developed in the laboratory to fit the particular requirements of the task. In attempting to synthesize PNIP, Dr. Nadizadeh initially used a conventional beta lactam method for which Dr. Holton had secured a patent, U.S. Patent No. 5,175,315 ("FSU '315 patent"). However, this beta lactam method resulted in undesired byproducts, and was not satisfactory. Over a period of four to five months, Dr. Nadizadeh worked to more effectively synthesize PNIP. As recorded in his lab books, this was a trial and error process in which he experienced numerous failures. Ultimately, on February 14, 1992, Dr. Nadizadeh successfully found a special beta lactam method that could be used to effectively

synthesize PNIP at high yields. On July 1, 1992, Dr. Nadizadeh submitted this taxol analog to BMS for biological testing.

In creating this new beta lactam, Dr. Nadizadeh made two changes to the conventional beta lactam method set forth in Dr. Holton's '315 patent. In general terms, the conventional method required the following four steps: (1) the imine formation and the 2 + 2 cyclo addition; (2) the ceric amonium nitrate ("CAN") reaction; (3) the base hydrolysis; and (4) the TES protection of the hydroxyl. Dr. Nadizadeh's special method moved the CAN reaction to the last step and used acid hydrolysis rather than base hydrolysis. Dr. Nadizadeh and his FSU team never published this special beta lactam method and there is no evidence that this method had ever been published in the public literature prior to February 14, 1992. A preponderance of the evidence at trial established that this special method for creating a beta lactam was not known outside of Dr. Holton's research team and constituted an FSU trade secret.

Of the hundreds of taxol analogs created and tested at FSU prior to Dr. Tao's departure, Dr. Holton testified that three specific constituents had proven to be the best when added at the N position of the side-chain. These three constituents were t-butoxy-carbonyl, isopropoxycarbonyl, and isobutoxycarbonyl. The t-butoxy-carbonyl was attached to the PNIP taxane made by Dr. Nadizadeh, and the isopropoxycarbonyl and isobutoxycarbonyl constituents were synthesized at the N position by Dr. Tao while working at FSU. As a result of his work at FSU, Dr. Tao was named as a co-inventor on a patent issued to FSU on April 14, 1998, U.S. Patent. No. 5,739,362 ("FSU '362 patent"). That patent covered the two compounds made by Dr. Tao at FSU with an isopropoxycarbonyl and an isobutoxycarbonyl, respectively, at the N position on the side-chain. The same patent also covered FSU's PNIP compound made by Dr. Nadizadeh.

On March 10, 1993, Dr. Li-Xi Yang, a well known radiation biologist originally from China, arrived at FSU as a courtesy professor. He had invented metra-nitizol, a substance used all over the world, and had an international reputation. Soon after

arriving at FSU, Dr. Yang met several of Dr. Holton's research assistants and learned of the taxol and taxol analog work that Dr. Holton was pursuing. Although radiation biology was his specialty, Dr. Yang was also an experienced chemist who during his career had developed several chemical compounds with increased radiosensitivity for anti-cancer applications. Since his early work in his native country of China, Dr. Yang had concentrated his research in increasing the radiosensitivity of hypoxic cells. These poorly oxygenated cancer cells are much more radio-resistant than the oxygenated cells closer to a blood vessel and are a major cause for the failure of radio-therapy. From his own review of the published literature, Dr. Yang was aware that taxol naturally possessed some radiosensitizing properties. In furtherance of his own research in radio-biology, Dr. Yang wanted to enhance the natural radiosensitivity of taxol to create a compound that would have both cytotoxic and radiosensitizing properties. He recognized that Dr. Holton's work might complement his own radio-biology research.

In July of 1993, Dr. Yang visited Dr. Holton in his office to discuss the idea of creating a chemotherapeutic radiosensitizing taxane ("CRT"). Dr. Yang believed that the dual functional characteristics of a CRT would prove to be a revolutionary step in the treatment of cancer. At their initial meeting, Dr. Holton cautioned Dr. Yang that the taxol structure was extremely difficult to modify and expressed doubts about the viability of Dr. Yang's idea. Nonetheless, he requested that Dr. Yang prepare a proposal and provide literature to support the idea of a CRT. By August of 1993, Dr. Yang had prepared a proposal for Dr. Holton setting forth the hypothesis of a CRT, a proposed testing schedule, and proposed the attachment of nitro electron affinic groups to taxol analogs to increase radiosensitivity.[6] Dr. Holton evaluated the proposal, and was surprised at the potential it held. In December of 1993, he decided

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[6]At this time, a great deal of literature existed on radiosentization and on the natural radiosensitivity of taxol. However, it is undisputed that the idea of attaching nitro electron affinic groups to a taxol analog to increase the radiosensitivity was not in the published literature.

to work with Dr. Yang in attempting to create a so-called CRT by synthesizing taxol analogs for Dr. Yang to test.

Dr. Holton assigned Dr. Nadizadeh the responsibility of synthesizing the compounds that Dr. Holton and Dr. Yang believed would prove to be effective CRTs, in particular, those involving the attachment of nitro electron affinic groups to taxol in an attempt to increase the compound's radiosensitivity. Initially, Dr. Nadizadeh synthesized taxol-METRO, which had metronidazole, a nitro group, attached at the C-7 position of the ring structure, rather than the typical hydroxyl. As previously noted, prior to either Dr. Yang or Dr. Tao's arrival, Dr. Nadizadeh had synthesized the PNIP compound as a part of the team's taxol analog efforts. After talking to Dr. Yang and reading his proposal, Dr. Holton determined that PNIP may possess the properties necessary to be an effective CRT. Therefore, he also had Dr. Nadizadeh provide that compound to Dr. Yang for testing.

Dr. Holton and Dr. Nadizadeh provided Dr. Yang a number of taxane compounds to test for enhanced radiosensitivity, but Dr. Yang determined that PNIP was clearly the best. As a result of his biological testing, Dr. Yang discovered that PNIP possessed a remarkable ability to kill certain types of cancer cells as a dual functional compound.[7] In light of these test results, on October 27, 1994, Dr. Holton sent a memorandum to Dr. Michael Devine, FSU's Assistant Director of Research, setting out the CRT invention developed at FSU. This memorandum was intended to initiate the process for obtaining a patent on CRTs. Eventually, on September 13, 1995, FSU filed its application for a patent on the concept of chemotherapeutic radiosensitizing taxanes, U.S. Application No. 09/129,647 ("FSU '647 application"), with the United States Patent and Trademark Office ("PTO").[8]

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[7]Although PNIP may be too toxic for human use at the present time, the initial testing by Dr. Yang suggests that the toxicity problems can be ameliorated.

[8]On September 13, 1995, FSU filed a provisional application, Serial No. 60/003,687. On September 13, 1996, FSU filed U.S. Patent Application Serial No.

The members of Dr. Holton's team, especially Dr. Tao, were interested in learning the results of Dr. Yang's tests on the taxol analogs. Dr. Yang often talked to team members in the chemistry building where he did some of his lab work. Both Dr. Holton and Dr. Yang considered Dr. Yang to be part of Dr. Holton's research team, and Dr. Yang felt free to discuss his research with Dr. Holton's research assistants. The evidence establishes that Dr. Tao either overheard or was involved in direct conversations about the CRT work being done by Dr. Nadizadeh, Dr. Holton, and Dr. Yang. Other than the evasive testimony given by Dr. Tao, all of the evidence demonstrates that the members of Dr. Holton's research team were aware of the research being done by the other team members. Dr. Tao obviously knew of Dr. Nadizadeh's PNIP taxane. Two facts are especially telling: first, Dr. Tao was named as a co-inventor on the FSU '362 patent that claimed this taxol analog; and second, on September 22, 1993, Dr. Tao was given a list of taxane compounds synthesized and tested by Dr. Holton's research team, which included FSU's PNIP. In light of these facts and Dr. Tao's knowledge of PNIP, it is highly improbable that Dr. Tao had not heard of Dr. Nadizadeh's special beta lactam method used to attach the side-chain to create the PNIP taxane, as he claims.[9] Moreover, Dr. Tao's knowledge of FSU's CRT project was further enhanced by the close relationship he developed with Dr. Yang.

08/710,240 ("FSU '240 application"), which claimed the priority date of the provisional application. On August 5, 1998, FSU filed U.S. Patent Application Serial No. 09/129,647 ("FSU '647 application"), which was a continuation of the prior FSU '240 application. Therefore, the FSU '647 application is entitled to the priority date of September 13, 1995.

[9]The mere fact that Dr. Tao arrived at FSU a few weeks after Dr. Nadizadeh synthesized the PNIP compound does not necessarily mean that he was unaware of the special beta lactam method that Dr. Nadizadeh employed. Based on the evidence presented at trial, it would have been nearly impossible for Dr. Tao to not have become aware of this method as a result of discussions between team members throughout his tenure at FSU.

Dr. Yang and Dr. Tao first met in June of 1993, when both were in Jacksonville, Florida, for their physical examinations required for their residency applications. While waiting outside the INS office, they met and learned that they were both doing research at FSU. The two spoke in their native language (Chinese) about the work that each was involved in at FSU. After this initial meeting, Dr. Yang spoke to Dr. Tao often on the FSU campus and in the chemistry building.[10] There is no doubt that Dr. Yang spoke with Dr. Tao about CRTs and the radiosensitivity of the taxol analogs that he was testing. Moreover, Dr. Yang told Dr. Tao and the other Holton team members that PNIP was the most effective CRT.[11] Dr. Yang also gave Dr. Tao literature on radiosensitization and explained the terminology, concepts, and rationale of radio-biology to Dr. Tao before he left FSU.[12] Dr. Yang shared this confidential information, especially about PNIP being the most effective CRT, with Dr. Tao because Dr. Tao was a member of Dr. Holton's analog project. Thus, as a result of his position of confidence at FSU, Dr. Tao obtained a vast amount of knowledge

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[10]In fact, Dr. Yang requested Dr. Tao's assistance in creating some compounds that Dr. Yang was unable to make. Although these compounds were not related to the CRT project, they dealt with the radiosensitivity testing that Dr. Yang was pursuing and provided Dr. Tao numerous opportunities to discuss Dr. Yang's work on CRTs.

[11]Dr. Tao testified that he never discussed these topics with Dr. Yang and that he only knew that Dr. Yang was conducting radiation testing. In both his deposition and at trial, Dr. Tao gave evasive answers and asserted that he new "nothing" while at FSU. I find that Dr. Tao's testimony in this respect is not credible. He plainly had a close relationship with Dr. Yang and they often discussed the work in which each was involved. Dr. Tao's pleas of ignorance are contradicted by the vast weight of the evidence presented at trial.

[12]Although Dr. Tao denies even knowing that Dr. Yang was working with CRTs, Dr. Tao knew that Dr. Yang was working on radiosensitization and he knew that Dr. Yang was testing some taxol compounds for Dr. Holton for radiosensitivity. Dr. Tao admits that he did a lot of literature searches while at FSU on the CRT concepts, which merely corroborates the fact that he had learned from Dr. Yang and discussed Dr. Yang's research.

about trade secrets and proprietary information related to the effectiveness of CRTs and the best way to synthesize such compounds. Dr. Tao took this knowledge with him when he left FSU.

In Dr. Holton's laboratory, it was normal for the post-doctoral research assistants to move on to other jobs in academia or in private industry after two to three years. This seems to be a standard practice at all research universities. Generally, when a research assistant began to interview for a new job, he or she would notify Dr. Holton and Dr. Holton would meet with the assistant to discuss what information and work could be disclosed to others and what was confidential to FSU. The evidence is not entirely clear as to when or how Dr. Tao informed Dr. Holton that he was moving to a different job. Dr. Holton testified that Dr. Tao simply stuck his head in Dr. Holton's office a couple of weeks before he left and said that he was going to a small company in California. However, Dr. Tao testified that he showed a slide presentation, which explained his work at FSU, to Dr. Holton before going to any interviews. During interviews, Dr. Tao intended to use this slide presentation to demonstrate his qualifications to potential employers, and he did so. It does not appear that Dr. Tao had a normal exit interview with Dr. Holton. The small company with whom Dr. Tao ultimately accepted a job was VivoRx, Inc., a pharmaceutical research company.

The Chief Executive Officer of VivoRx, Inc. was Dr. Patrick Soon-Shiong, a medical doctor and surgeon. The company was pursuing various avenues of research that concentrated on diabetes and cancer treatments.[13] As early as 1992, Dr. Soon-Shiong and the company's Senior Research Scientist, Dr. Neil Desai, attended a

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[13]Initially, Dr. Soon-Shiong was the Chairman and Chief Executive Officer of VivoRx Pharmaceuticals, Inc. ("VPI"), which was the predecessor entity to American Bioscience, Inc. He has held the same positions in ABI since its inception in 1994. When the patent at issue was originally applied for, Dr. Soon-Shiong was VPI's only employee on paper. Other employees of the separate company, VivoRx, Inc. ("VI"), were assigned to work for VPI, as well as for VI. VI concentrated on diabetes research, while VPI focused on cancer research.

conference on taxol at which the natural radiosensitivity of taxol was discussed.[14] After attending this conference, Dr. Soon-Shiong and Dr. Desai, both of whom are well-trained and accomplished scientists, discussed the potential of creating a taxol analog from a compound called taxotere, which they believed might possess greater radiosensitivity than taxol itself. However, these conversations were general and preliminary in nature, and the record is clear that neither they, nor anyone else at VivoRx, had the background or skill to successfully synthesize such a compound. Nonetheless, Dr. Desai began to read a great deal of literature on taxol and radiosensitization.[15] Dr. Desai testified that, based on the inherent radiosensitivity of taxol, Dr. Soon-Shiong and he believed that the dual properties of cytotoxicity and radiosensitivity would be present in such compounds. However, prior to November of 1994, neither Dr. Soon-Shiong nor Dr. Desai had seen any literature that discussed the use of a taxol analog as a chemotherapeutic radiosensitizing taxane, and neither individual knew the chemical structure of any such compound at that time. Moreover, no one at VivoRx had ever done any bench work in an attempt to synthesize a taxane with such dual functional properties.[16] Prior to Dr. Tao's arrival, the extent of the

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[14]This conference was hosted by the National Cancer Institute and was billed as the Second NCI Workshop on Taxol and Taxus. Def. Ex. 2221. Dr. Soon-Shiong testified that the individuals speaking at this conference were all of the leading names in taxol research. It was after attending this conference that Dr. Soon-Shiong and Dr. Desai began to formulate their plan to pursue research on taxol analogs as radiosensitizers. Although Dr. Soon-Shiong initially denied having any substantive knowledge of Dr. Holton or his taxol-related work, he ultimately acknowledged that Dr. Holton spoke at this NCI conference on the synthesis of taxol, and Dr. Soon-Shiong admitted that he probably was present during Dr. Holton's presentation.

[15]Dr. Desai (who was the most credible of the defendants' witnesses) is a native of India and has a Ph.D. in chemical engineering from the University of Texas. His primary area of work has been in diabetes treatment.

[16]Prior to Dr. Tao's arrival, the only bench work done on taxol analogs at VivoRx was by Dr. Desai on the water solubility of taxol analogs for a drug delivery system. VivoRx obtained a patent on this work. Def. Ex. 2295.

research done by Dr. Soon-Shiong and Dr. Desai on the concept of CRTs was merely to become familiar with the prior art on taxol and radiosensitization.[17]

In August 1994, Dr. Soon-Shiong received a job application letter that Dr. Tao had sent to a different company, which had been forwarded to Dr. Soon-Shiong because it was known that he was looking for new scientists interested in cancer research. After receiving this letter, Dr. Soon-Shiong called Dr. Tao. During their conversation, Dr. Soon-Shiong explained that his company was doing diabetes and encapsulation research and had a strategy to pursue cancer research as well. Ultimately, VivoRx invited Dr. Tao to California for an interview in October of 1994. During this interview, Dr. Tao presented his slide presentation and described his taxol analog research at FSU. At this time, VivoRx had no involvement with taxol-related research and had neither the expertise nor the equipment and materials to pursue the ideas that Dr. Desai and Dr. Soon-Shiong had discussed in 1992. However, Dr. Tao provided VivoRx with an opportunity to hire an organic chemist with a ground-breaking research background in taxol and taxol analog synthesis. Dr. Soon-Shiong seized this opportunity and offered Dr. Tao a job, which he accepted.

On November 16, 1994, after Dr. Tao's interview, Dr. Neil Desai recorded notes in his lab book from a planning meeting with Dr. Soon-Shiong. Pl. Ex. 52. In these notes, there is a notation of taxol derivatives and radiation sensitizers being discussed. However, no details were provided. These notes are the first documentation that anyone at VivoRx had ever considered the possibility of making taxol analogs as radiosensitizers. The next day, on November 17, 1994, VivoRx ordered one gram of a taxol compound called 10-DAB from Dabur India, Ltd.[18] However, no one at VivoRx

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[17]It appears that scientists in the United States and other countries were considering ways to improve and build on the recognized natural radiosensitivity of taxol. However, the means for accomplishing that goal remained unclear.

[18]While attending a professional conference in India, Dr. Desai had spoken to representatives of Dabur India about supplying 10-DAB to VivoRx.

had ever worked with 10-DAB and this order was not received until after Dr. Tao arrived. In his deposition, Dr. Paul Sandford, who was Dr. Desai's superior at VivoRx, testified that he did not participate in any discussions concerning dual functioning taxanes until after Dr. Tao arrived at VivoRx, and the project to create such taxanes did not begin until after Dr. Tao's arrival.[19]

When Dr. Tao arrived at VivoRx in December of 1994, Dr. Desai provided him with what he had located in the published literature on radiosensitizers and immediately assigned him the task of creating a chemotherapeutic radiosensitizing taxane. Dr. Desai testified that his primary contribution to this project was making Dr. Tao familiar with the prior art. Although Dr. Desai was responsible for the final decision on what compounds to pursue, he and Dr. Tao discussed the possible changes that could be made at the N position of the side-chain after modifying the 3' position. Without doubt, Dr. Tao's experience and knowledge from FSU were the basis of these initial decisions. No one else at VivoRx had sufficient background in the CRT area to provide meaningful guidance. Moreover, Dr. Tao conducted all of the bench work for the patent that was ultimately obtained by VivoRx. Dr. Tao frankly admitted that he believed that he could use any information, confidential or otherwise, that he obtained from FSU in his work at VivoRx.[20] Implied in that admission is the fact that he did so.

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[19]Dr. Sandford testified that he advised Dr. Soon-Shiong against hiring Dr. Tao because VivoRx was not involved in substantive taxol research and lacked the necessary equipment to work in that area. Dr. Sandford also stated that he had been denied access to several files concerning Dr. Tao's employment and work at VivoRx, which subsequently disappeared while under the control of Dr. Soon-Shiong.

[20]Neither Dr. Soon-Shiong nor Dr. Desai took any precautions to ensure that Dr. Tao honored any confidential obligations that he may have owed to FSU. In fact, the evidence in the record strongly suggests that Dr. Soon-Shiong hired Dr. Tao because of his knowledge of taxol analogs gained at FSU. Dr. Soon-Shiong simply left for Dr. Tao to determine what could and could not be used at VivoRx. In so acting, Dr. Soon-Shiong may have taken advantage of Dr. Tao's failure to comprehend the ethical rules and culture that apply in the American scientific community.

The evidence plainly demonstrates that Dr. Tao utilized confidential information from FSU in synthesizing the three specific compounds that are claimed in the ultimate patent obtained by VivoRx. Specifically, Dr. Tao used the special beta lactam method developed by Dr. Nadizadeh for attaching the PNIP side-chain to the taxol ring structure, which constituted the use of an FSU trade secret. Dr. Tao's notebook from VivoRx shows essentially the same method as the special method developed by Dr. Nadizadeh.[21] Pl. Ex. 32. On December 14, 1994, Dr. Tao started making the necessary beta lactam; and by December 21, 1994, he had completed it. Thus, Dr. Tao came straight into the laboratory at VivoRx and completed in a matter of days (and without any unsuccessful trials) the same reaction that took Dr. Nadizadeh five months of trial and error to achieve. Dr. Tao's testimony that he had never seen or heard of this beta lactam method at FSU and that he was able to immediately perform the same reaction is not credible.[22] Dr. Tao also used his knowledge and experience from FSU in selecting and attaching the isopropoxycarbonyl and isobutoxycarbonyl at the N position of the side-chain, which involved the proprietary information of FSU. In his work at VivoRx, Dr. Tao used a taxotere molecule, which is commercially available 10-DAB. When Dr. Nadizadeh first made FSU's PNIP, he used Baccatin III as a starting material, which FSU referred to as "taxoltere." The only difference

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[21]The '653 patent included a schematic at figure 6, scheme 5, which revealed Dr. Nadizadeh's beta lactam method.

[22]Dr. Tao testified that he had done a great deal of reading on this issue. However, that fails to explain his ability to replicate the work previously done at FSU in an extraordinarily short period of time. Notably, Dr. Tao's lab book does not reflect any failed reactions. Pl. Ex. 32. Moreover, any variations between Dr. Nadizadeh's beta lactam and that reflected in Dr. Tao's lab book are minor and may be the result of the fact that Dr. Tao was attempting to perform the reaction from memory. Dr. Tao clearly was able to recall the four basic steps used by Dr. Nadizadeh, even if he could not recall the exact amounts of acid or solvent that Dr. Nadizadeh used. Although Dr. Tao may have eventually been able to re-create this beta lactam on his own, it is unrealistic to believe that he did so in a mere eight days without relying on the work previously done by Dr. Nadizadeh at FSU.

between taxoltere and taxotere was that taxoltere had an acetate rather than a hydroxyl at the C-10 position due to the starting material used.[23]

On June 7, 1995, VivoRx Pharmaceuticals, Inc. filed U.S. Patent Application Serial No. 485,496 ("'496 application"), entitled "Nitrophenyl, Pen-Deacetlyated Substituted Taxol Derivatives as Dual-Functional Cytotoxic Radiosensitizers." Pl. Ex. 152. The '496 application named as inventors: Chunlin Tao, Neil P. Desai, Patrick Soon-Shiong, and Paul A. Sandford.[24] In filing this application, the named inventors submitted an oath in which they declared that they were the original, true, and correct

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[23]Taxotere is a variation of taxol patented by Aventis, a French pharmaceutical company. In 1994, Dr. Soon-Shiong directed Dr. Desai to begin creating analogs of taxotere. The starting material for taxotere is 10-DAB. The PNIP taxane created by Dr. Nadizadeh differed in two particulars from taxotere. First, taxotere has a phenyl group at the 3' position; and second, it has an hydroxyl at the C-10 position. In contrast, PNIP has a paranitrophenyl ring at the 3' position and an acetate at the C-10 position. The compound at the C-10 position is a result of the starting material used. The two standard starting materials for making synthetic taxol were Baccatin III and 10-DAB. Generally, 10-DAB was a preferred starting material because it was commercially available, as opposed to Baccatin III which had to be made by cleaving the side-chain from taxol and was not commercially available. In contrast to Baccatin III, 10-DAB is made from the needles of the English Yew tree, which is common in Europe and India. Thus, 10-DAB comes from a renewable resource, is available in larger supplies at a lower cost, and does not involve the environmental ramifications of taxol. FSU began using 10-DAB as a starting material when it became commercially available from BMS, who served as FSU's supplier.

Dr. Nadizadeh explained that PNIP can be synthesized using either Baccatin III or 10-DAB as a starting material. Using 10-DAB requires protection of the starting material at both the C-7 and the C-10 positions because both of these positions have an hydroxyl. The side-chain must connect to the ring structure at the C-13 position, which also is an hydroxyl. Because the side-chain will attempt to connect to the C-7 and C-10 positions, these positions must be masked/protected before the attachment of the side-chain can be attempted. In contrast, Baccatin III only requires protection at the C-7 position because the C-10 position on Baccatin III is an acetate.

[24]When VivoRx re-filed the same original patent application in 1998, Dr. Sandford had been deleted as an inventor. Pl. Ex. 46. Dr. Sandford testified that he did not contribute to the inventions claimed in the '653 patent, even though he was named as a co-inventor.

inventors of all of the claims originally presented in the '496 application. This patent application disclosed the generic concept of attaching electron affinic substituents to a taxane compound to impart radiosensitizing properties. The application also disclosed, and originally claimed, method and compound claims directed to dual-function taxanes having cytotoxic and radiosensitizing properties. Thus, this original application sought patent protection for the broad method of use concept (i.e. the introduction of an electron affinic group to a cytotoxic agent resulting in a radiosensitizer) and for specific chemical compositions.[25]

Dr. Stephan Reiter was the patent attorney who prepared the patent application for VivoRx. Dr. Reiter testified that he had no contact with Dr. Tao in the preparation of this patent.[26] Although it is unclear how information passed from Dr. Tao to Dr. Reiter, it must be inferred that Dr. Tao prepared all of the detailed specifications on these compounds because he was the only person at VivoRx with knowledge of how to synthesize these compounds. Presumably, Dr. Tao prepared a summary of his work, possibly with the assistance of Dr. Desai, by using the confidential information he obtained from FSU.[27] Dr. Reiter could not recall what he was told by Dr. Soon-

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[25]The patent application itself contained no data to support its representation that the claimed compounds would in fact possess dual properties. In fact, no such research had been done by VivoRx prior to filing this patent application. The defendants presented evidence that they rushed to file the patent application to take advantage of the grandfather clause provided by the GATT treaty, which recalculated the date from which patent protection would begin to run. Dr. Soon-Shiong and Dr. Desai testified that, based on the literature, they "expected" these dual functional properties to be present. However, after filing the patent application, their preliminary tests conducted on these compounds proved to be inconclusive. Based on the evidence at trial, it appears that Dr. Tao divulged to Dr. Soon-Shiong and Dr. Desai the success of Dr. Yang's radiosensitivity testing at FSU.

[26]Dr. Tao testified that he may have participated in a conference call with Dr. Reiter.

[27]No such report was produced during this litigation. However, it is possible that such a report was included in Dr. Sandford's files, which have "disappeared" at

Shiong and Dr. Desai concerning the inventorship of the '653 patent, and he did not maintain any records on that issue. Dr. Reiter was never told by Dr. Soon-Shiong or Dr. Desai that Dr. Tao had worked for Dr. Holton at FSU. Dr. Reiter acknowledged that he would have done further investigation into the issue of inventorship had he known of Dr. Tao's prior experience in Dr. Holton's laboratory. Even after the PTO rejected the original claims as being anticipated by the prior art of Dr. Holton, neither Dr. Soon-Shiong nor Dr. Desai told Dr. Reiter of Dr. Tao's prior employment. Dr. Reiter also noted that the utility of the compounds claimed in the patent application was their dual functional properties.

In an 'office action,' dated July 5, 1996, the PTO rejected all of VivoRx's outstanding claims. Def. Ex. 2217E. Specifically, the PTO found that the broad claim to CRTs was anticipated by existing literature, and in particular that a taxotere analog modified with a nitrophenyl group inherently possessed radiosensitizing properties. In rejecting these claims, the PTO specifically cited patents issued to Dr. Holton. Following this action, VivoRx amended its claims by abandoning its broad claims to CRTs (method of use claims) and by pursuing a patent on eight specific chemical compositions (composition of matter claims). Def. Ex. 2217F. VivoRx never filed a traverse or engaged in any of the customary back and forth discourse with the PTO in an effort to have the broad CRT claims allowed. Its strategy of moving speedily forward on its composition of matter claims was successful. On July 14, 1998, a patent was issued on three of the eight compounds claimed: (1) 3'-desphenyl-3'-(4-nitrophenyl)-N-debenzoyl-N-(t-butoxy-carbonyl)-10-deacetyltaxol; (2) 3'-desphenyl-3'-(4-nitrophenyl)-N-debenzoyl-N-(isopropoxycarbonyl)-10-deacetyltaxol; (3) 3'-desphenyl-3'-(4-nitrophenyl)-N-debenzoyl-N-(isobutoxycarbonyl)-10-deacetyltaxol. Pl. Ex. 152. (See diagram of compounds, Attachment B).

On September 13, 1995, approximately one month after VivoRx filed its patent application, Dr. Holton and his associates at FSU filed their patent application for

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VivoRx.

chemotherapeutic radiosensitizing taxanes, which described the class of compounds that were the subject matter of the '653 patent ultimately issued to VivoRx. The PTO has rejected FSU's claims and has cited the '653 patent as prima facie prior art under Title 35, United States Code, Section 102(e).[28] After engaging in discussions with the PTO, FSU has been advised that the '653 patent is the only prior art preventing a patent from issuing on FSU's patent application for CRTs.

II. CONCLUSIONS OF LAW

A. Inventorship

The ultimate issue in this case is whether Dr. Holton, Dr. Nadizadeh, and Dr. Yang were joint inventors of the three compounds claimed in the '653 patent.[29] The issuance of a patent creates a presumption that the named inventors are the true and only inventors of the subject matter of the patent. See Ethicon, Inc. v. United States Surgical Corp., 135 F.3d 1456, 1460 (Fed. Cir. 1998). However, this presumption is rebuttable, and a party or parties challenging inventorship can seek to have other inventors named as co-inventors on the patent. "To show co-inventorship, . . . the

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[28]Section 102(e) provides in pertinent part:

> A person shall be entitled to a patent unless--
> (e) The invention was described in--
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent. . . ; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent . . ..

[29]As set forth in the '653 patent, the inventorship of these compounds comes down to the person or persons who originally contributed to the answer of two key questions:

> In the preparation of derivative of therapeutic agents bearing electron affinic groups (e.g., paclitaxel), two questions needed to be addressed: selection of the electron affinic group(s), and the selection of the site of attachment to the therapeutic agent.

Pl. Ex. 43 at column 8.

alleged co-inventor or co-inventors must prove their contribution to the conception of the claims by clear and convincing evidence." Ethicon, Inc., supra, 135 F.3d at 1461. To satisfy this burden, the alleged co-inventor must produce evidence to corroborate his own testimony. See id.. "Whether the inventor's testimony has been sufficiently corroborated is evaluated under a 'rule of reason' analysis. Under this analysis, '[a]n evaluation of all pertinent evidence must be made so that a sound determination of the credibility of the [alleged] inventor's story may be reached.'" Id. (emphasis original) (quoting Price v. Symsek, 988 F.2d 1187, 1195 (Fed. Cir. 1993)). Corroborating evidence may come in the form of contemporaneous documents prepared by the alleged inventor, circumstantial evidence about the inventive process, or oral testimony from someone other than the alleged inventor. See id.. However, it is not necessary to corroborate every factual issue contested by the parties. See id. at 1464.

"A joint invention is the product of collaboration between two or more persons working together to solve the problem addressed." Burroughs Wellcome Co. v. Barr Laboratories, Inc., 40 F.3d 1223, 1227 (Fed. Cir. 1994). "Conception is the touchstone of inventorship, the completion of the mental part of invention." Id. at 1227-28. "Conception is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." Id. at 1228 (citing Sewall v. Walters, 21 F.3d 411, 415 (Fed. Cir. 1994)). Because of the mental nature of conception, it is necessary for a party claiming to be an inventor to present corroborating evidence, preferably of a contemporaneous disclosure, that would enable one skilled in the art to make the invention. See id.. The Federal Circuit has noted:

> An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention. These rules ensure that patent rights attach only when an idea is so far

> developed that the inventor can point to a definite, particular invention.

Id. (citations omitted). The "[c]onception of a chemical substance includes knowledge of both the specific chemical structure of the compound and an operative method for making it." Id. at 1229.

It is not necessary for joint inventors to physically work together, to work at the same time, to make the same type or amount of contribution, or to contribute to every claim in the patent. See 35 U.S.C. §116. Each of the joint inventors need only perform a part of the task which produces the invention, but a party's mere assistance to the actual inventor after conception is insufficient to constitute joint inventorship. See Ethicon, Inc., supra, 135 F.3d at 1460. Likewise, "[o]ne who simply provides the inventor with well-known principles or explains the state of the art without ever having a 'firm and definite idea' of the claimed combination as a whole does not qualify as a joint inventor." Id.. "[T]he qualitative contribution of each collaborator is the key - - - each inventor must contribute to the joint arrival at a definite and permanent idea of the invention as it will be used in practice." Id.. Thus, inventorship requires that two determinations be made: (1) what was the contribution made by the purported co-inventor, and (2) whether that contribution appears in the claimed invention. See id. at 1461.

Initially, clear and convincing evidence demonstrates that Dr. Holton, Dr. Yang, and Dr. Nadizadeh contributed to the invention of the patented compounds made by Dr. Tao at VivoRx. First, the evidence establishes that it was at Dr. Holton's direction and in collaboration with Dr. Holton at FSU that Dr. Tao learned about the effectiveness of and the method for attaching isopropoxycarbonyl and isobutoxycarbonyl at the N position of the side-chain of a taxol analog.[30] Moreover,

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[30]Although Dr. Tao's work at FSU with these constituents was not directly related to the CRT project, the effectiveness of these compounds and the method for attachment was proprietary information that contributed to two of the compounds claimed in the '653 patent.

Dr. Holton determined which taxol analogs were likely to possess the dual properties of a CRT, and Dr. Holton's unique knowledge of the taxol structure was critical to the pursuit of Dr. Yang's idea. Second, due to the position of confidence that he held at FSU, Dr. Tao learned of Dr. Nadizadeh's creation of PNIP and the special beta lactam he developed to most effectively attach the PNIP side-chain.[31] Third, Dr. Tao learned the concept and the specifics of a CRT from Dr. Yang; and as a result of Dr. Yang's testing, Dr. Tao learned that PNIP was the most effective CRT. The work of each of these individuals is corroborated by the memorandum sent to Dr. Devine on October 27, 1994, as well as by their lab books and the evidence presented on the inventive process at FSU. Therefore, Dr. Holton, Dr. Yang, and Dr. Nadizadeh contributed to the ultimate inventions claimed in the '653 patent. Dr. Tao merely continued at VivoRx the work that he observed being done by his former colleagues at FSU.

Furthermore, the contributions made by Dr. Holton, Dr. Yang, and Dr. Nadizadeh appear in the inventions claimed in the '653 patent. While at FSU and in collaboration with Dr. Holton, Dr. Tao created taxol analogs with isopropoxycarbonyl and isobutoxycarbonyl attached at the N position of the side-chain, which were included in the FSU '362 patent. Pl. Ex. 22 at 3. These constituents were the same as the distinguishing constituents in the second and third compounds claimed in the '653 patent. Moreover, the side-chain on FSU's PNIP created by Dr. Nadizadeh, which included a paranitrophenyl ring at the 3' position and a t-butoxy-carbonyl at the N position of the side-chain, is exactly the same side-chain as the one on the first compound claimed in the '653 patent. PNIP also was included in the FSU '362 patent,

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[31]Although the defendants argue that various beta lactam methods existed in the prior art that could have been used by Dr. Tao, the evidence clearly shows that Dr. Tao used the special method developed by Dr. Nadizadeh, as opposed to any alternative methods. Dr. Tao's VivoRx lab book shows that he used an acid hydrolysis and moved the CAN reaction of the last step, as previously done by Dr. Nadizadeh. Dr. Tao's after the fact rationalization as to why he used this method is not credible and fails to establish that his use of this method was not influenced by the knowledge he acquired while at FSU.

on which Dr. Tao was named as a co-inventor.[32] Furthermore, the '653 patent is laced throughout with language about the three compounds possessing the dual functional properties of cytotoxicity and radiosensitivity. Dr. Tao learned of this concept from Dr. Yang at FSU. It was Dr. Yang's testing that proved that PNIP was an effective chemotherapeutic radiosensitizing taxane.[33] Therefore, the contributions of Dr. Holton, Dr. Yang, and Dr. Nadizadeh appear in the claimed inventions.[34]

Moreover, it has been shown by clear and convincing evidence that Dr. Soon-Shiong, Dr. Desai, and Dr. Sandford did not contribute to the inventions claimed in the '653 patent. First, Dr. Desai acknowledged that his primary contribution to the invention was providing Dr. Tao with literature and explaining to him the state of the art on radiosensitizers and on taxol's natural radiosensitivity. At the time that Dr. Desai made these contributions, he lacked a firm and definite idea as to how a taxane with dual functional properties could be made. Such an alleged contribution is insufficient to qualify as a joint inventor. See Ethicon, Inc., supra, 135 F.3d at 1460 (noting that explanation of prior art without firm idea of claimed combination is

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[32]It is clear that the novelty of the first compound claimed in the '653 patent was the side-chain, which was made at FSU by Dr. Nadizadeh in 1992. In fact, the only characteristic that distinguishes FSU's PNIP from the first compound in the '653 patent is the constituent at the C-10 position. However, this is a distinction without a difference because it was merely a result of the starting material used. Dr. Nadizadeh made FSU's PNIP with Baccatin III before 10-DAB was readily available.

[33]The defendants have attempted to assert that this patent is simply a composition of matter patent and any dual functional properties that might exist are immaterial. This argument is disingenuous. Throughout the patent and the original patent application, the applicants repeatedly refer to these compounds as potential chemotherapeutic radiosensitizers, and Dr. Reiter, the patent attorney who drafted the patent application, testified that these dual properties were key to the utility of the claimed compounds.

[34]It is only necessary that these individuals made a contribution to the claimed inventions, and it is immaterial that these three specific compounds were never actually made at FSU. See Ethicon, Inc., supra, 135 F.3d at 1460.

insufficient for co-inventorship). Dr. Soon-Shiong's contribution was even less than that of Dr. Desai. As with Dr. Desai, Dr. Soon-Shiong merely had the abstract idea of increasing the radiosensitivity of taxol analogs. No evidence was presented on any specific recommendations or suggestions that he may have made in furtherance of this idea. The only contributions that he appears to have made were the decisions to hire Dr. Tao to pursue this line of research and to use taxotere. However, in reality, this latter decision was merely a decision to use commercially available 10-DAB. Dr. Sandford admitted in his deposition that he did not make any contribution to this invention, and he subsequently was removed as a named inventor when the same application was re-filed in 1998.

It has also been proven by clear and convincing evidence that the conception of the first compound claimed in the '653 patent was completed at FSU before Dr. Tao even arrived at VivoRx. Because 10-DAB and Baccatin III are essentially interchangeable starting materials, Dr. Nadizadeh and Dr. Holton obviously knew that 10-DAB could be used to create FSU's PNIP and they knew how to reduce that knowledge to practice. Even assuming that Dr. Soon-Shiong and Dr. Desai had discussed a goal of attempting to create the first compound in the '653 patent, they did not know how to reduce it to practice without extensive research and experimentation. See Burroughs Wellcome Co., supra, 40 F.3d at 1228-30 (finding that conception requires ability to reduce invention to practice without extensive research or experimentation). This lack of knowledge was the reason that they hired Dr. Tao. Moreover, the conception of the second and third compounds essentially involved the additional decision to attach isopropoxycarbonyl and isobutoxycarbonyl to the N position of the side-chain. The placement of these compounds at the N position had already been conceived of by Dr. Holton and reduced to practice at FSU by Dr. Tao. The decision to use these compounds at VivoRx to create CRTs was a decision made by Tao based on the knowledge that he had obtained from FSU. For all of these reasons, Dr. Soon-Shiong, Dr. Desai, and Dr. Sandford were not true and

rightful co-inventors of the compounds claimed in the '653 patent.[35]

"[I]f nonjoinder of an actual inventor is proved by clear and convincing evidence, a patent is rendered invalid," pursuant to Title 35, United States Code, Section 102(f).[36] Pannu v. Iolab Corp., 155 F.3d 1344, 1349 (Fed. Cir. 1998) (internal citations omitted). "However, in cases of misjoinder and nonjoinder the operation of section 102(f) is ameliorated by section 256." Id. at 1350. Section 256 allows a party that has proven by clear and convincing evidence to have been an unnamed co-inventor to save the patent from invalidity by having the court correct the named inventors on the patent. See 35 U.S.C. §256. However, the party alleging to have been the co-inventor must demonstrate that "the error occurred without any deceptive intent on the part of the unnamed inventor." Pannu, supra, 155 F.3d at 1350. Due to the difficulty in showing the lack of deceptive intent, "good faith is presumed in the absence of a persuasive showing of deceptive intent." Id. at 1350 n.4.

It has been shown by clear and convincing evidence that the '653 patent names the incorrect inventors of the chemical compounds claimed therein. Moreover, no evidence has been presented to show that the failure to name the correct inventors occurred with any deceptive intent on the part of Dr. Holton, Dr. Yang, or Dr. Nadizadeh; and the good faith of these individuals is presumed. Pursuant to section 256, Dr. Holton, Dr. Yang, and Dr. Nadizadeh shall be added to the '653 patent as co-inventors; and Dr. Soon-Shiong, Dr. Desai, and Dr. Sandford shall be removed as inventors. I further conclude that Dr. Holton and his research team at FSU conceived and reduced to practice at FSU both the class of compounds described in the FSU

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[35]To the extent that these individuals at VivoRx contributed to the creation of the claimed compounds, they merely provided assistance to Dr. Tao after the conception of the inventions. See Ethicon, Inc., supra, 135 F.3d at 1460 (finding assistance after conception insufficient for co-inventorship).

[36]Section 102(f) provides that a person is not entitled to a patent if "he did not himself invent the subject matter sought to be patented."

'647 application,[37] including specifically N-debenzoyl-N-(t-butylcarbomoyl)-7-(metronidazoleoxycarbonyl) taxol and N-debenzoyl-N-(t-butylcarbomoyl)-3'-desphenyl-3-(4-nitrophenyl) taxol, sometimes referred to as CRTs, and the use of these compounds in a process to treat cancer cells, prior to the time that Dr. Tao and this associates at VivoRx conceived of any subject matter disclosed in the '653 patent. Dr. Holton, Dr. Yang, and Dr. Nadizadeh are the first, true, and rightful inventors of such subject matter vis-a-vis Dr. Tao, Dr. Soon-Shiong, Dr. Desai, and Dr. Sandford.

B. Inequitable Conduct

The second issue to be resolved in this case is whether the '653 patent should be rendered unenforceable due to inequitable conduct by the inventors named on the patent. A person guilty of inequitable conduct in obtaining a patent may be precluded from enforcing any rights under the patent ultimately obtained. See 37 C.F.R. §1.56. If a patent is unenforceable due to inequitable conduct, then the patent may not be enforced even by 'innocent' co-inventors. See Stark v. Advanced Magnetics, Inc., 119 F.3d 1551, 1556 (Fed. Cir. 1996). "Inequitable conduct includes affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive." Molins PLC, v. Textron, Inc., 48 F.3d 1172, 1178 (Fed. Cir. 1995). After the threshold determination of materiality and intent to deceive have been made, the court must determine whether the conduct was so culpable as to render the patent unenforceable. See PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc., 225 F.3d 1315, 1319 (Fed. Cir. 2000).

There are three elements to the threshold finding of inequitable conduct. First, the information withheld or misrepresented must have been material. Second, the applicant must be charged with knowledge of the information and its materiality. Third, the applicant must have misrepresented or have failed to disclose the information with the intent to mislead the PTO. See Molins PLC, supra, 48 F.3d at

[37]This application was a continuation of the provisional FSU '240 application.

1178. The plaintiffs have satisfied each of these elements by clear and convincing evidence.

First, "[i]nformation is 'material' when there is a substantial likelihood that a reasonable examiner would have considered the information important in deciding whether to allow the application to issue as a patent."[38] Id. at 1179. In addressing the materiality issue, the appropriate standard is whether the information would have been important to a 'reasonable examiner;' and the Federal Circuit has recognized that "[a]s a critical requirement for obtaining a patent, inventorship is material." PerSeptive Biosystems Inc., supra, 225 F.3d at 1321; see also Molins PLC, supra, 48 F.3d at 1179. It is undisputed that the applicants did not name Dr. Holton, Dr. Yang, or Dr. Nadizadeh as co-inventors. Moreover, the patent application incorrectly named Dr. Soon-Shiong, Dr. Desai, and Dr. Sandford as inventors. The evidence demonstrates that Dr. Soon-Shiong, as the head of the company, and Dr. Desai, as the liaison between the company and the patent attorney, deliberately avoided telling their attorney of Dr. Tao's prior employment at FSU, which initially was a more material omission than FSU's actual contribution to the inventions. Therefore, the applicants made material misrepresentations and omissions in their application for the '653 patent.

Second, the applicants can be charged with knowledge that the true inventors

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[38] PTO Rule 56 [37 C.F.R. §1.56] defines material information as follows:

> (b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and,
>
> (1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or
>
> (2) It refutes, or is inconsistent with, a position the applicant takes in:
>
> (i) Opposing an argument of unpatentability relied on by the Office, or
>
> (ii) Asserting an argument of patentability.

of these compounds included the scientists at FSU. Clearly, Dr. Tao knew of the contributions made by Dr. Holton, Dr. Yang, and Dr. Nadizadeh. Moreover, Dr. Soon-Shiong and Dr. Desai knew that Dr. Tao had been employed in Dr. Holton's laboratory at FSU, where he worked with and acquired extensive knowledge on taxol and taxol analogs. Therefore, Dr. Soon-Shiong and Dr. Desai can be charged with knowledge that scientists at FSU contributed to their claimed inventions.

Third, the deceptive intent of the applicants may be inferred from the facts and circumstances surrounding the applicants' conduct. "Intent need not be proven by direct evidence; it is most often proven by a showing of acts, the natural consequences of which are presumably intended by the actor." Molins PLC, supra, 48 F.3d at 1180. The showing of deceptive intent must be made by clear and convincing evidence, and gross negligence alone will not suffice as a showing of the requisite intent. See id. at 1181; Kingsdown Medical Consultants, Ltd. v. Hollister, Inc., 863 F.2d 867, 876 (Fed. Cir. 1988).

> Thus, the alleged conduct must not amount merely to the improper performance of, or omission of, an act one ought to have performed. Rather, clear and convincing evidence must prove that an applicant had the specific intent to accomplish an act that the applicant ought not to have performed, viz., misleading or deceiving the PTO. In a case involving nondisclosure of information, clear and convincing evidence must show that the applicant made a deliberate decision to withhold a known material reference.

Molins, PLC, supra, 48 F.3d at 1181.

It has been proven by clear and convincing evidence that the applicants on the '653 patent acted with the intent to deceive the PTO when they made material misrepresentations and omissions about the inventorship of the claimed compounds. See PerSeptive Biosystems, Inc., supra, 225 F.3d at 1319-22. Several circumstances demonstrate the applicants' deceptive intent. First, neither Dr. Soon-Shiong nor Dr. Desai disclosed to their patent attorney, Dr. Reiter, that Dr. Tao previously had worked with Dr. Holton on taxol analogs; and they continued to withhold this information from

their patent attorney, even after the PTO rejected their original claims on the ground that Dr. Holton's work was prior art. The withholding of Dr. Tao's link to FSU indicates that Dr. Soon-Shiong and Dr. Desai wanted to avoid any issues that would arise from such a disclosure. Second, Dr. Tao signed an oath of inventorship with full knowledge of the contributions made by the scientists at FSU and without disclosing that information to Dr. Reiter or to the PTO. Likewise, Dr. Soon-Shiong and Dr. Desai signed the oath of inventorship with knowledge of Dr. Tao's prior employment at FSU and with reason to believe that the patent application claimed inventions to which the scientists at FSU contributed. Under these circumstances, the failure of Dr. Soon-Shiong and Dr. Desai to make an inquiry into FSU's contributions amounted to deliberate avoidance of the truth, and not merely a negligent failure to act.

"Once threshold findings of materiality and intent are established, the court must weigh them to determine whether the equities warrant a conclusion that inequitable conduct occurred." Molins PLC, supra, 48 F.3d at 1178. "The more material the conduct, the less evidence of intent will be required in order to find that inequitable conduct has occurred." PerSeptive Biosystems, Inc., supra, 225 F.3d at 1319. "In determining inequitable conduct, a trial court may look beyond the final claims to their antecedents." Fox Indus., Inc. v. Structural Preservation Systems, Inc., 922 F.2d 801, 803 (Fed. Cir. 1990); see also PerSeptive Biosystems, Inc., supra, 225 F.3d at 1322 (recognizing that inventorship of patents actually issued does not limit material misrepresentations of inventorship previously made in application). "In light of all the circumstances, an equitable judgment must be made concerning whether the applicant's conduct is so culpable that the patent should not be enforced." Molins PLC, supra, 48 F.3d at 1178.

Based on the above findings of fact and conclusions of law, I conclude that the conduct of Dr. Soon-Shiong, Dr. Desai, and Dr. Tao was so culpable as to render the '653 patent unenforceable. Representations as to the true and rightful inventors of the subject matter of the patent were of the utmost materiality, and Dr. Tao's link to

FSU makes suspect all representations that the invention of these compounds at VivoRx was totally independent of any contributions from FSU. By not disclosing Dr. Tao's prior relationship with Dr. Holton at FSU, Dr. Soon-Shiong and Dr. Desai purposefully withheld material information on the issue of inventorship from their patent attorney and, consequently, from the PTO for the purpose of misleading the PTO on the inventorship of the three compounds claimed in the '653 patent.[39] Dr. Tao's misrepresentations and omissions as to inventorship were by far the most material because he had firsthand knowledge of the contributions made by the scientists at FSU. However, due to his poor understanding of the ethical standards in this country and clear lack of knowledge about the United States patent system, his intent to deceive may not have been as egregious as that of his superiors at VivoRx, who appear to have taken advantage of Dr. Tao's naivete. Thus, in light of the clear and convincing evidence of material misrepresentations and omissions and of deceptive intent on the part of the patent applicants, I find that the '653 patent must be, and is, declared unenforceable.

III. CONCLUSION

For the reasons set forth above, it is hereby ORDERED and DECLARED:

A. Dr. Holton and his research team at FSU conceived and reduced to practice both the class of compounds and the use of these compounds as chemotherapeutic radiosensitizing taxanes, as described in the FSU '647 application, prior to the time such subject matter was conceived by Dr. Tao, Dr. Soon-Shiong, Dr. Desai, and (if applicable) Dr. Sandford.

B. Dr. Holton, Dr. Yang, and Dr. Nadizadeh are true and rightful co-inventors

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[39]I also note that the applicants engaged in inequitable conduct as to the broader method of use claims related to CRTs, which were included in the original application and subsequently were abandoned. These broader method of use claims were interrelated with the specific composition of matter claims that ultimately were allowed by the PTO. Although not an essential factor, the inequitable conduct as to these broader claims is relevant to a finding of inequitable conduct as to the specific claims on which the patent issued.

of the subject matter in the '653 patent and should be added to the patent as such.

C. Dr. Soon-Shiong and Dr. Desai (and Dr. Sandford, to the extent he may still be considered as a co-inventor) are not true and rightful co-inventors of the subject matter in the '653 patent and their names should be removed from the patent.

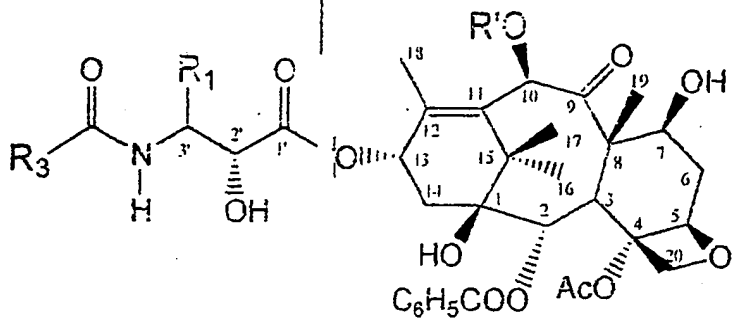
D. Due to inequitable conduct by the applicants during the application process, the '653 patent is hereby declared unenforceable.

The Clerk shall enter judgment accordingly, together with taxable costs.

DONE AND ORDERED this 31st day of October, 2001.

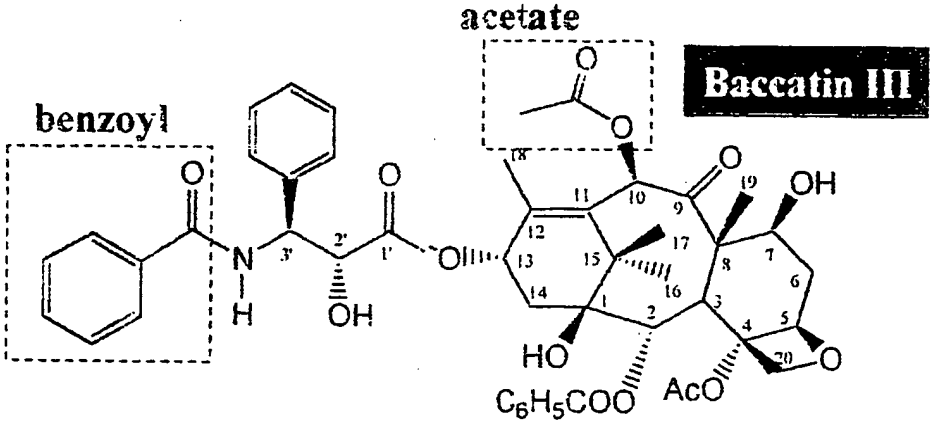
ROGER VINSON
Chief United States District Judge

GENERAL TAXANE STRUCTURE

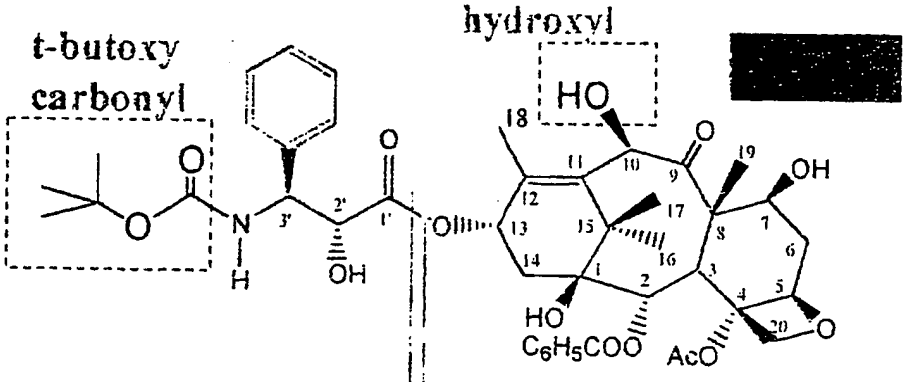


β-Lactam Side Chain | Taxane ring

TAXOL (BRISTOL MYERS SQUIBB)



TAXOTERE (AVENTIS)



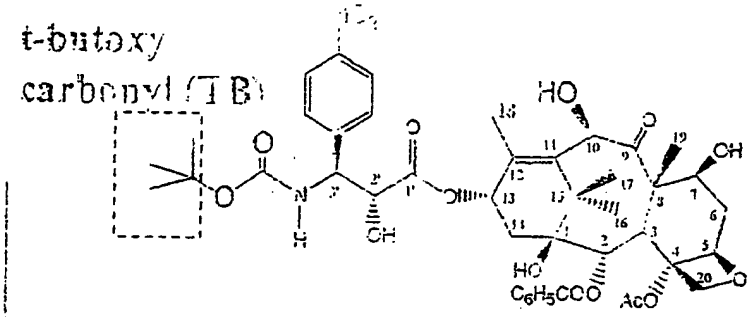
ATTACHMENT A

2746

[redacted]

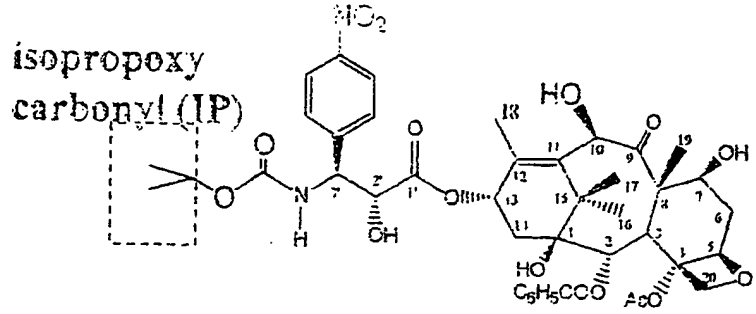
ABI-1

β-Lactam (TB-nitro) + [redacted] → **ABI-1**



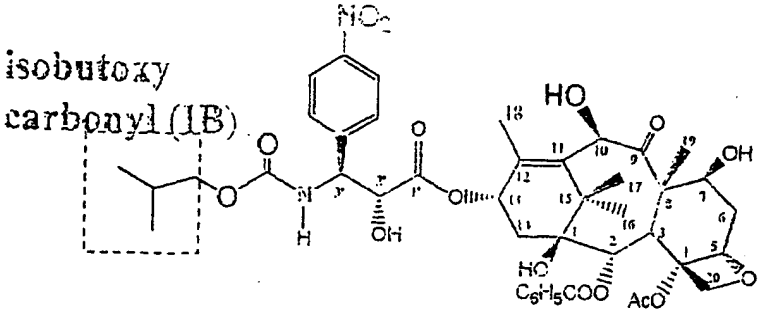
ABI-2

β-Lactam (IP- nitro) + [redacted] → **ABI-2**



ABI-3

β-Lactam (IB- nitro) + [redacted] → **ABI-3**



2747

ATTACHMENT B